```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 3106900061...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 01.08.22D

Last logoff:  25sep01 14:54:31
Logon file405 25sep01 17:46:04
KWIC is set to 50.
HILIGHT set on as '*'
PICKS is set ON as an alias for 5,55,159,143,358,340,344,348,351,352,447,72,73,154,1
55,349.
* * *
SYSTEM:HOME
Menu System II: D2 version 1.7.8 term=ASCII
                    *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

    (c) 2000  The Dialog Corporation plc      All rights reserved.

      /H = Help           /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
?S denatured collagen
>>Invalid Option Number

                    *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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```

/H = Help = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
?s denatured collagen
>>Invalid Option Number

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG(R) Document Delivery
7. Data Star(R)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
?b picks

>>> 351 is unauthorized
>>> 352 is unauthorized
>>>2 of the specified files are not available
25sep01 17:47:22 User243038 Session D77.1
$0.00 0.209 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.10 TYMNET
$0.10 Estimated cost this search
$0.10 Estimated total session cost 0.209 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2001/Sep W3
(c) 2001 BIOSIS
File 55:Biosis Previews(R) 1993-2001/Sep W3
(c) 2001 BIOSIS
File 159:Cancerlit 1975-2001/Aug
(c) format only 2001 Dialog Corporation
***File 159: This file has been reloaded. Accession Numbers have changed.**
File 143:Biol. & Agric. Index 1983-2001/Aug
(c) 2001 The HW Wilson Co
File 358:Current BioTech Abs 1983-2001/Aug
(c) 2001 DECHEMA
***File 358: Updates delayed. Please see HELP NEWS 358 for details.**
File 340:CLAIMS(R)/US PATENT 1950-01/Sep 18
(c) 2001 IFI/CLAIMS(R)
***File 340: Price changes as 0f 1/1/01. Please see HELP RATES 340.**
File 344:CHINESE PATENTS ABS APR 1985-2001/Aug
(c) 2001 EUROPEAN PATENT OFFICE
File 348:EUROPEAN PATENTS 1978-2001/Sep W02
(c) 2001 European Patent Office
File 447:IMSWorld Patents International 2001/Sep
(c) 2001 IMSWorld Publ. Ltd.
File 72:EMBASE 1993-2001/Sep W3
(c) 2001 Elsevier Science B.V.
***File 72: For information about Explode feature please**
see Help News72.

File 73:EMBASE 1974-200[redacted]ep W3
(c) 2001 Elsevier Science B.V.
*File 73: For information about Explode feature please see Help News73.
File 154:Medline(R) 1990-2001/Oct W3
File 155:MEDLINE(R) 1966-2001/Oct W3
File 349:PCT Fulltext 1983-2001/UB=20010913, UT=20010906
(c) 2001 WIPO/MicroPat

Set	Items	Description

?s denatured collagen?
S1 14 DENATURED COLLAGEN?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S2 7 RD (unique items)
?s s2 and antagonist?
7 S2
1240661 ANTAGONIST?
S3 0 S2 AND ANTAGONIST?
?s s2 and antibod?
7 S2
2455234 ANTIBOD?
S4 1 S2 AND ANTIBOD?
?t s4/5/all

4/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08553903 BIOSIS NO.: 199344103903
The role of the MHC class I region and the conformation of the antigen in resistance to collagen arthritis in rhesus monkeys.
AUTHOR: Jonker Margaret; Bontrop Ronald E; 'T Hart Bert A; Bakker Koos P M
AUTHOR ADDRESS: Dep. Chroic Infect. Dis., ITGRI, TNO, PO Box 5815, 22280 HV Rijswik**Netherlands Antilles
JOURNAL: Journal of Cellular Biochemistry Supplement 0 (17 PART B):p134 1993
CONFERENCE/MEETING: Keystone Symposium on Molecular Mechanisms in Rheumatoid Arthritis and Related Disease Keystone, Colorado, USA January 31-February 7, 1993
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Immune System (Chemical Coordination and Homeostasis); Pathology; Skeletal System (Movement and Support)
BIOSYSTEMATIC NAMES: Cercopithecidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Cercopithecidae (Cercopithecidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; nonhuman primates; primates; vertebrates
MISCELLANEOUS TERMS: ABSTRACT; *DENATURED COLLAGEN TYPE II*; IMMUNOGLOBULIN M *ANTIBODY*; IMMUNOREGULATION; MAJOR HISTOCOMPATIBILITY COMPLEX CLASS I ALLELE; T CELL
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal

```
  10506   Biophysics-Molecular Properties and Macromolecules
  12508   Pathology, General and Miscellaneous-Inflammation and
            Inflammatory Disease
  15004   Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
  15008   Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and
            Reticuloendothelial System
  18006   Bones, Joints, Fasciae, Connective and Adipose Tissue-Pathology
  34508   Immunology and Immunochemistry-Immunopathology, Tissue Immunology
  00520   General Biology-Symposia, Transactions and Proceedings of
            Conferences, Congresses, Review Annuals
  10062   Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
  10064   Biochemical Studies-Proteins, Peptides and Amino Acids
  10068   Biochemical Studies-Carbohydrates
BIOSYSTEMATIC CODES:
  86205   Cercopithecidae
?ds

Set     Items   Description
S1         14   DENATURED COLLAGEN?
S2          7   RD (unique items)
S3          0   S2 AND ANTAGONIST?
S4          1   S2 AND ANTIBOD?
?s s7 and type I
>>>"S7" does not exist
                0  S7
             1370  TYPE I
      S5        0  S7 AND TYPE I
?s s2 and type I
                7  S2
             1370  TYPE I
      S6        0  S2 AND TYPE I
?s collagen type I
      S7     1088  COLLAGEN TYPE I
?s s7 and antagonist?
             1088  S7
          1240661  ANTAGONIST?
      S8       20  S7 AND ANTAGONIST?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S9       10  RD (unique items)
?t s8 and denatured
>>>'AND' not allowed in command
?s s8 and denatur?
                20  S8
            186596  DENATUR?
     S10        0  S8 AND DENATUR?
?s s8 and antibod?
                20  S8
           2455234  ANTIBOD?
     S11        2  S8 AND ANTIBOD?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S12        1  RD (unique items)
```

?t s12/5/all

12/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11940609 BIOSIS NO.: 199900186718
Blocking angiotensin II ameliorates proteinuria and glomerular lesions in progressive mesangioproliferative glomerulonephritis.
AUTHOR: Nakamura Takamichi(a); Obata Jun-ei; Kimura Hideaki; Ohno Shinichi; Yoshida Yoji; Kawachi Hiroshi; Shimizu Fujio
AUTHOR ADDRESS: (a)Division of Blood Transfusion, Yamanashi Medical University, 1110 Shimokato Tamaho, Nakakoma, Ya**Japan
JOURNAL: Kidney International 55 (3):p877-889 March, 1999
ISSN: 0085-2538
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background. The renin-angiotensin system is thought to be involved in the progression of glomerulonephritis (GN) into end-stage renal failure (ESRF) because of the observed renoprotective effects of angiotensin-converting enzyme inhibitors (ACEIs). However, ACEIs have pharmacological effects other than ACE inhibition that may help lower blood pressure and preserve glomerular structure. We previously reported a new animal model of progressive glomerulosclerosis induced by a single intravenous injection of an anti-Thy-1 monoclonal *antibody*, MoAb 1-22-3, in uninephrectomized rats. Using this new model of progressive GN, we examined the hypothesis that ACEIs prevent the progression to ESRF by modulating the effects of angiotensin II (Ang II) on the production of transforming growth factor-beta (TGF-beta) and extracellular matrix components. Methods. We studied the effect of an ACEI (cilazapril) and an Ang II type 1 receptor *antagonist* (candesartan) on the clinical features and morphological lesions in the rat model previously reported. After 10 weeks of treatment with equihypotensive doses of cilazapril, cilazapril plus Hoe 140 (a bradykinin receptor B2 *antagonist*), candesartan, and hydralazine, we examined systolic blood pressure, urinary protein excretion, creatinine clearance, the glomerulosclerosis index, and the tubulointerstitial lesion index. We performed a semiquantitative evaluation of glomerular immunostaining for TGF-beta and collagen types I and III by immunofluorescence study and of these cortical mRNA levels by Northern blot analysis. Results. Untreated rats developed massive proteinuria, renal dysfunction, and severe glomerular and tubulointerstitial injury, whereas uninephrectomized control rats did not. There was a significant increase in the levels of glomerular protein and cortical mRNA for TGF-beta and collagen types I and III in untreated rats. Cilazapril and candesartan prevented massive proteinuria, increased creatinine clearance, and ameliorated glomerular and tubulointerstitial injury. These drugs also reduced levels of glomerular protein and cortical mRNA for TGF-beta and collagen types I and III. Hoe 140 failed to blunt the renoprotective effect of cilazapril. Hydralazine did not exhibit a renoprotective effect. Conclusion. These results indicate that ACEIs prevent the progression to ESRF by modulating the effects of Ang II via Ang II type 1 receptor on the production of TGF-beta and collagen types I and III, as well as on intrarenal hemodynamics, but not by either increasing bradykinin activity or reducing blood pressure in this rat model of mesangial proliferative GN.

REGISTRY NUMBERS: 11128-99-7: ANGIOTENSIN II; 88768-40-5: CILAZAPRIL; 9015-82-1: ANGIOTENSIN-CONVERTING ENZYME; 139481-59-7: CANDESARTAN; 58-82-2: BRADYKININ
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Pharmacology; Urinary System (Chemical Coordination and Homeostasis)
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: rat (Muridae)--animal model

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
DISEASES: end-stage renal failure--urologic disease; mesangioproliferative glomerulonephritis--urologic disease; proteinuria--urologic disease
CHEMICALS & BIOCHEMICALS: angiotensin II; candesartan--angiotensin II type 1 receptor *antagonist*; cilazapril--angiotensin-converting enzyme inhibitor-drug; *collagen type I*; collagen type III; transforming growth factor beta; Hoe 140--bradykinin receptor B2 *antagonist*
METHODS & EQUIPMENT: Northern blot analysis--analytical method
MISCELLANEOUS TERMS: renin angiotensin system
ALTERNATE INDEXING: Kidney Failure, Chronic (MeSH); Proteinuria (MeSH)
CONCEPT CODES:
22002 Pharmacology-General
10060 Biochemical Studies-General
12502 Pathology, General and Miscellaneous-General
15501 Urinary System and External Secretions-General; Methods
BIOSYSTEMATIC CODES:
86375 Muridae
?ds

Set	Items	Description
S1	14	DENATURED COLLAGEN?
S2	7	RD (unique items)
S3	0	S2 AND ANTAGONIST?
S4	1	S2 AND ANTIBOD?
S5	0	S7 AND TYPE I
S6	0	S2 AND TYPE I
S7	1088	COLLAGEN TYPE I
S8	20	S7 AND ANTAGONIST?
S9	10	RD (unique items)
S10	0	S8 AND DENATUR?
S11	2	S8 AND ANTIBOD?
S12	1	RD (unique items)

?s s7 and non-peptidic compound

	1088	S7
	0	NON-PEPTIDIC COMPOUND
S13	0	S7 AND NON-PEPTIDIC COMPOUND

?s s7 and oligonucleotide?

	1088	S7
	245388	OLIGONUCLEOTIDE?
S14	6	S7 AND OLIGONUCLEOTIDE?

?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S15 3 RD (unique items)
?t s15/5/all

15/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12850976 BIOSIS NO.: 200100058125
Antisense basic fibroblast growth factor *oligonucleotide* reduced adhesion of retinal pigment epithelial cells to extracellular matrix molecules and their proliferation.
AUTHOR: Rho Sae Heun; Yoon Hee Seong; Yoo Kyung Won; Park Woo Chan; Jeong Jin Hee; Yoo Young Hyun(a)
AUTHOR ADDRESS: (a)Department of Anatomy and Cell Biology, Dong-A University College of Medicine, 3-1 Dondaesin-Dong, Seo-Gu, Pusan,

602-103: yhyoo@daunet.do[redacted].ac.kr**South Korea
JOURNAL: Ophthalmic Research 33 (1):p24-30 January-February, 2001
MEDIUM: print
ISSN: 0030-3747
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We investigated the effect of extracellular matrix molecules on the adhesion of retinal pigment epithelial cells and their subsequent proliferation. Fibronectin, collagen type I and vitronectin enhanced their adhesion and proliferation. In addition, the effect of basic fibroblast growth factor (bFGF) on their adhesion and proliferation was studied. bFGF enhanced their adhesion and proliferation, whereas antisense bFGF reduced their adhesion to and their proliferation on extracellular matrix molecules.

REGISTRY NUMBERS: 106096-93-9: BASIC FIBROBLAST GROWTH FACTOR
DESCRIPTORS:
MAJOR CONCEPTS: Sense Organs (Sensory Reception)
BIOSYSTEMATIC NAMES: Suidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: pig (Suidae)--animal model
ORGANISMS: PARTS ETC: retinal pigment epithelial cells--cultured, extracellular matrix adhesion, proliferation, sensory system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Artiodactyls; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
CHEMICALS & BIOCHEMICALS: antisense basic fibroblast growth factor *oligonucleotide*; basic fibroblast growth factor; *collagen type I*; fibronectin; vitronectin
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02506 Cytology and Cytochemistry-Animal
20004 Sense Organs, Associated Structures and Functions-Physiology and Biochemistry
BIOSYSTEMATIC CODES:
85740 Suidae

15/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11196467 BIOSIS NO.: 199799817612
Down-regulation of the amyloid protein precursor of Alzheimer's disease by antisense *oligonucleotides* reduces neuronal adhesion to specific substrate.
AUTHOR: Coulson Elizabeth J; Barrett Graham L; Storey Elsdon; Bartlett Perry F; Beyreuther Konrad; Masters Colin L(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Univ. Melbourne, Parkville, VIC 30052** Australia
JOURNAL: Brain Research 770 (1-2):p72-80 1997
ISSN: 0006-8993
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The hallmark of Alzheimer's disease is the cerebral deposition of amyloid which is derived from the amyloid precursor protein (APP). The function of APP is unknown but there is increasing evidence for the role of APP in cell-cell and/or cell-matrix interactions. Primary cultures of murine neurons were treated with antisense *oligonucleotides* to down-regulate APP. This paper presents evidence that APP mediates a substrate-specific interaction between neurons and extracellular matrix components collagen type I, laminin and heparan sulphate proteoglycan but not fibronectin or poly-L-lysine. It remains to be determined whether this effect is the direct result of APP-matrix interactions, or whether

an intermediary pathway [redacted] involved.

REGISTRY NUMBERS: 11061-24-8: AMYLOID; 25104-18-1Q: POLY-L-LYSINE; 38000-06-5Q: POLY-L-LYSINE
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology); Nervous System (Neural Coordination)
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: murine (Muridae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
CHEMICALS & BIOCHEMICALS: AMYLOID; POLY-L-LYSINE
MISCELLANEOUS TERMS: Research Article; ALZHEIMER'S DISEASE; AMYLOID; AMYLOID PROTEIN PRECURSOR; ANTISENSE *OLIGONUCLEOTIDES*; BEHAVIORAL AND MENTAL DISORDERS; CELL-CELL INTERACTIONS; CELL-MATRIX INTERACTIONS; *COLLAGEN TYPE I*; FIBRONECTIN; HEPARAN SULFATE PROTEOGLYCAN; LAMININ; NERVOUS SYSTEM; NERVOUS SYSTEM DISEASE; NEURONAL ADHESION; NEURONS; POLY-L-LYSINE
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
10506 Biophysics-Molecular Properties and Macromolecules
10508 Biophysics-Membrane Phenomena
20504 Nervous System-Physiology and Biochemistry
20506 Nervous System-Pathology
BIOSYSTEMATIC CODES:
86375 Muridae

15/5/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08831724 BIOSIS NO.: 199395121075
Serum and tissue protein binding and cell surface properties of Staphylococcus lugdunensis.
AUTHOR: Paulsson Marianne; Petersson Ann-Cathrine; Ljungh Asa(a)
AUTHOR ADDRESS: (a)Dep. Med. Microbiology, Univ. Lund, Solvegatan 23, S-22362 Lund**Sweden
JOURNAL: Journal of Medical Microbiology 38 (2):p96-102 1993
ISSN: 0022-2615
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Eleven strains of Staphylococcus lugdunensis from different clinical sources were investigated for their ability to bind 125I-labelled collagen (Cn) type I and IV, fibronectin (Fn), vitronectin (Vn), laminin (Lm), fibrinogen (Fg), thrombospondin, plasminogen (glu- and lys-form) and human IgG. All the strains bound these proteins, although a higher degree of binding was obtained for Cn types I and IV and IgG with mean values of 36%, and 26% binding, respectively. In tests with proteins immobilised on latex beads in a particle agglutination assay, eight of the 11 strains bound Cn type I and seven bound Fg, whereas no strain bound immobolised IgG. Binding to immobilised Cn-I, Fg, Lm and Vn was abolished when the bacterial cells were treated with proteases or heat, indicating cell-surface receptors with protein characteristics. Cell-surface extracts of S. lugdunensis 2342 were able to totally inhibit binding of the homologous strain and S. aureus Cowan 1 to latex-immobilised proteins Cn-I, Lm, Vn, Fn and Fg. The binding of 125I-labelled Cn IV by S. lugdunensis 2342, was heat sensitive, whereas the binding to S. aureus Cowan 1 was heat resistant. The strains gave negative results in tests for the presence of protein A with a S. aureus protein A gene probe and with sensitised red blood cells. No production

of heat-stable nuclease [redacted]ase) could be detected by mono[redacted]nal antibodies against TNase or by the polymerase chain reacti[redacted] with an *oligonucleotide* sequence from S. aureus TNase as primer. When the cell surface characters of the S. lugdunensis strains were studied, five were found to be hydrophobic and negatively charged, four hydrophilic and positively charged and two hydrophobic with positive net charge.

REGISTRY NUMBERS: 9026-81-7: NUCLEASE
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics (Transport and Circulation); Cell Biology; Infection; Membranes (Cell Biology); Metabolism
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Micrococcaceae--Eubacteria, Bacteria
ORGANISMS: human (Hominidae); Staphylococcus aureus (Micrococcaceae); Staphylococcus lugdunensis (Micrococcaceae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; bacteria; chordates; eubacteria; humans; mammals; microorganisms; primates; vertebrates
CHEMICALS & BIOCHEMICALS: NUCLEASE
MISCELLANEOUS TERMS: ADHERENCE; CELL SURFACE RECEPTORS; *COLLAGEN TYPE I*; COLLAGEN TYPE IV; FIBRINOGEN; FIBRONECTIN; HEAT-STABLE NUCLEASE; IMMUNOGLOBULIN G; LAMININ; PLASMINOGEN; PROTEIN A; THROMBOSPONDIN; VITRONECTIN
CONCEPT CODES:
10508 Biophysics-Membrane Phenomena
13012 Metabolism-Proteins, Peptides and Amino Acids
15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
30500 Morphology and Cytology of Bacteria
36002 Medical and Clinical Microbiology-Bacteriology
02508 Cytology and Cytochemistry-Human
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
10808 Enzymes-Physiological Studies
31000 Physiology and Biochemistry of Bacteria
34502 Immunology and Immunochemistry-General; Methods
34504 Immunology and Immunochemistry-Bacterial, Viral and Fungal
BIOSYSTEMATIC CODES:
07702 Micrococcaceae (1992-)
86215 Hominidae

```
?s denatured collagen type I
     S16       0  DENATURED COLLAGEN TYPE I
?s denatur? collagen type I
     S17       0  DENATUR? COLLAGEN TYPE I
?ds

Set     Items   Description
S1         14   DENATURED COLLAGEN?
S2          7   RD (unique items)
S3          0   S2 AND ANTAGONIST?
S4          1   S2 AND ANTIBOD?
S5          0   S7 AND TYPE I
S6          0   S2 AND TYPE I
S7       1088   COLLAGEN TYPE I
S8         20   S7 AND ANTAGONIST?
S9         10   RD (unique items)
S10         0   S8 AND DENATUR?
S11         2   S8 AND ANTIBOD?
S12         1   RD (unique items)
S13         0   S7 AND NON-PEPTIDIC COMPOUND
S14         6   S7 AND OLIGONUCLEOTIDE?
S15         3   RD (unique items)
S16         0   DENATURED COLLAGEN TYPE I
S17         0   DENATUR? COLLAGEN TYPE I
?s reduced affinity
     S18       2  REDUCED AFFINITY
?s s18 and s1
               2  S18
```

```
          14  S1
     S19       0  S18 AND
?s s7 and monoclonal antibod?
>>>File 5 processing for MONOCLONAL ANTIBOD? stopped at MONOCLONAL ANTIBODY
   1B3
>>>File 55 processing for MONOCLONAL ANTIBOD? stopped at MONOCLONAL
   ANTIBODY 1B3
>>>File 72 processing for MONOCLONAL ANTIBOD? stopped at MONOCLONAL
   ANTIBODY ME 1
>>>File 73 processing for MONOCLONAL ANTIBOD? stopped at MONOCLONAL
   ANTIBODY L72
        1088  S7
      155864  MONOCLONAL ANTIBOD?
     S20       2  S7 AND MONOCLONAL ANTIBOD?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S21       1  RD (unique items)
?t s21/5/all

 21/5/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

11709068   BIOSIS NO.: 199800490799
```
Monoclonal antibodies directed against extracellular matrix proteins reduce the adherence of Candida albicans to HEp-2 cells.
```
AUTHOR: Cotter Gary; Weedle Roisin; Kavanagh Kevin(a)
AUTHOR ADDRESS: (a)Med. Mycology Unit, Dep. Biology, National Univ.
  Ireland, Maynoonth, Co. Kildare**Ireland
JOURNAL: Mycopathologia  141 (3):p137-142 1998
ISSN: 0301-486X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The presence of the extracellular matrix (ECM) proteins collagen
  types I and IV, laminin and fibronectin on the surface of HEp-2 cells was
  confirmed by flow cytometry using monoclonal antibodies. Monoclonal
  antibodies directed against these ECM proteins reduced the adherence of
  C. albicans ATCC 44990 to HEp-2 cells, the greatest reductions being
  evident in assays which incorporated anti-collagen type IV monoclonal
  antibody. The ability of sugaramines to inhibit the adherence of C.
  albicans to a variety of cell types has been demonstrated previously and
  the most significant reduction in C. albicans - HEp-2 adherence was in
  assays which incorporated 0.2 M galactosamine. The combination of
  anti-collagen IV monoclonal antibody and galactosamine reduced the
  adherence of C. albicans to HEp-2 cells by approximately 70% (p < 0.05).

REGISTRY NUMBERS: 7535-00-4: GALACTOSAMINE
DESCRIPTORS:
  MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Mycology
  BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
    Animalia; Osteichthyes--Pisces, Vertebrata, Chordata, Animalia
  ORGANISMS: Candida-albicans (Osteichthyes)--adherence;  HEp-2 (Hominidae)
  BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Fish;
    Humans; Mammals; Nonhuman Vertebrates; Primates; Vertebrates
  CHEMICALS & BIOCHEMICALS:   *collagen type I*--extracellular matrix
    protein;  collagen type IV--extracellular matrix protein;  fibronectin
    --extracellular matrix protein;  galactosamine;  laminin--extracellular
    matrix protein;  *monoclonal antibodies*
```

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CONCEPT CODES:
  10060   Biochemical Studies-General
  34502   Immunology and Immunochemistry-General; Methods
  50506   Botany, General and Systematic-Fungi
BIOSYSTEMATIC CODES:
  85206   Osteichthyes
  86215   Hominidae
?ds

Set     Items   Description
S1         14   DENATURED COLLAGEN?
S2          7   RD (unique items)
S3          0   S2 AND ANTAGONIST?
S4          1   S2 AND ANTIBOD?
S5          0   S7 AND TYPE I
S6          0   S2 AND TYPE I
S7       1088   COLLAGEN TYPE I
S8         20   S7 AND ANTAGONIST?
S9         10   RD (unique items)
S10         0   S8 AND DENATUR?
S11         2   S8 AND ANTIBOD?
S12         1   RD (unique items)
S13         0   S7 AND NON-PEPTIDIC COMPOUND
S14         6   S7 AND OLIGONUCLEOTIDE?
S15         3   RD (unique items)
S16         0   DENATURED COLLAGEN TYPE I
S17         0   DENATUR? COLLAGEN TYPE I
S18         2   REDUCED AFFINITY
S19         0   S18 AND S1
S20         2   S7 AND MONOCLONAL ANTIBOD?
S21         1   RD (unique items)
?s angiogenesis
     S22   86193  ANGIOGENESIS
?s s22 and s7
           86193  S22
            1088  S7
     S23      22  S22 AND S7
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S24      11  RD (unique items)
?s s24 and antagonist?
              11  S24
         1240661  ANTAGONIST?
     S25       0  S24 AND ANTAGONIST?
?t s24/5/all

 24/5/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13090401   BIOSIS NO.: 200100297550
```
The anti-angiogenic effect of halofuginone (Halo): Inhibition of collagen type I tube formation, matrix metalloproteinase-2 (MMP-2) activities and extracellular matrix (ECM) deposition.

AUTHOR: Nagler A(a); Elkin E; Miao H-Q; Reich R; Pines M; Vlodavsky I
AUTHOR ADDRESS: (a)BMT, Hadassah**Israel
JOURNAL: Blood 96 (11 Part 1):p34a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society [redacted] Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: *Angiogenesis* is essential for the growth and spread of hematooncological tumors. It is a multifactorial process involving type I collagen tube formation which directs the migration and assembly of endothelial cells, MMP-2 degradation of ECM proteins including collagen and new capillary basement membrane (BM)-like ECM deposition. Halo, a low molecular weight (495Da) quinazolinone alkaloid was previously shown by us to inhibit collagen alpha1 (I) gene expression and synthesis. We therefore hypothesized that Halo may inhibit *angiogenesis*. We evaluated the potential antiangiogenic effect of Halo both in vitro and in vivo using several assays: 1) Capillary-like tube formation with Bovine aortic and human umbilical endothelial cells. 2) Rat aortic ring microvessel formation and 3) Murine micropocket bFGF induced corneal *angiogenesis*. In vitro in the presence of Halo (50 ng/ml) both bovine and human endothelial cells lost their ability to form new capillary vessels and appeared as unorganized cell aggregates. Similarly Halo (100ng/ml) completely inhibited microvessel formation from rat aortic rings embedded in collagen type I gel. As collagen type I is one of the major constituents of the stroma we evaluated the effect of Halo on ECM deposition by cultured vascular endothelial cells assessed by incorporation of radiolabeled sulfate. Eighty five percent inhibition of ECM deposition was observed in cultures incubated with 50ng/ml Halo. In addition microscopic examinations of the denuded culture dishes revealed a very thin or no ECM. We next evaluated the effect of Halo on MMP-2 enzymatic activity by vascular endothelial cells and demonstrated an almost complete inhibition of MMP-2 expression and enzymatic activity as well as BM invasion by 100ng/ml Halo. Finally, in vivo Halo administered either P.O (5mg/kg) or I.P. (2mg/mouse/day) for 7 days caused profound inhibition of bFGF induced corneal neovascularization in the murine micropocket corneal *angiogenesis* model (the area of neovascularization was reduced from 1.7+0.3 mm2 to 0.6+0.2 mm2 in the control and Halo (either P.O or I.P) treated mice, respectively. In summary, Halo inhibits several steps in the angiogenetic process: MMP-2 expression and BM invasion, capillary-like tube formation and vascular sprouting as well as deposition of subendothelial ECM and finally bFGF induced neovascularization in vivo. This makes Halo a promising candidate for further evaluation in anti-angiogenic therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE; 146480-35-5: MATRIX METALLOPROTEINASE-2
DESCRIPTORS:
MAJOR CONCEPTS: Immune System (Chemical Coordination and Homeostasis); Pharmacology
BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: bovine (Bovidae); human (Hominidae); mouse (Muridae); rat (Muridae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Artiodactyls; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: *collagen type I*; halofuginone--anti-angiogenic effect, antineoplastic-drug; matrix metalloproteinase-2
MISCELLANEOUS TERMS: *angiogenesis*; collagen type I tube formation--inhibition; extracellular matrix deposition; Meeting Abstract
CONCEPT CODES:
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10802 Enzymes-General and Comparative Studies; Coenzymes

12512 Pathology, Gener[redacted]and Miscellaneous-Therapy (197[redacted])
22002 Pharmacology-Gen[redacted]al
22005 Pharmacology-Clinical Pharmacology (1972-)
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
85715 Bovidae
86215 Hominidae
86375 Muridae

24/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12977402 BIOSIS NO.: 200100184551
The micro-ecosystem of primary cancer invasion: Cancer cells, host cells and extracellular matrix.
AUTHOR: Mareel M(a)
AUTHOR ADDRESS: (a)Ghent University Hospital, Ghent**Belgium
JOURNAL: European Journal of Cancer 36 (Supplement 5):pS27-S28 September, 2000
MEDIUM: print
CONFERENCE/MEETING: 2nd European Breast Cancer Conference Brussels, Belgium September 26-30, 2000
ISSN: 0959-8049
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
REGISTRY NUMBERS: 9004-61-9: HYALURONAN
DESCRIPTORS:
MAJOR CONCEPTS: Cell Biology; Tumor Biology
BIOSYSTEMATIC NAMES: Animalia
ORGANISMS: animal (Animalia)
ORGANISMS: PARTS ETC: endothelial cells; extracellular matrix; fibroblasts; immunocytes--immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals
DISEASES: cancer--neoplastic disease, primary invasion, progression
CHEMICALS & BIOCHEMICALS: E-cadherin; beta-catenin; *collagen type I*; fibronectin; hyaluronan; laminin; nidogen
MISCELLANEOUS TERMS: *angiogenesis*; cancer cell-host cell interaction; micro-ecosystem; signal transduction; Meeting Paper
ALTERNATE INDEXING: Neoplasms (MeSH)
CONCEPT CODES:
02502 Cytology and Cytochemistry-General
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
02506 Cytology and Cytochemistry-Animal
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
24003 Neoplasms and Neoplastic Agents-Immunology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
34502 Immunology and Immunochemistry-General; Methods
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
33000 Animalia-Unspecified

24/5/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12738040 BIOSIS NO.: 200000491663
Collagen type I: A substrate and a signal for invasion.
BOOK TITLE: Progress in Molecular and Subcellular Biology; Signaling through the cell matrix
AUTHOR: Van Hoorde Leen(a); Van Aken Elisabeth; Mareel Marc(a)

BOOK AUTHOR/EDITOR: Maciei[redacted]Coelho Alvaro: Author
AUTHOR ADDRESS: (a)Laborato[redacted]y of Experimental Cancerology, [redacted]partment of Radiotherapy and Nuclear Medicine, Ghent University Hospital, De Pintelaan 185, 9000, Gent**Belgium
JOURNAL: Progress in Molecular and Subcellular Biology 25p105-134 2000
MEDIUM: print
BOOK PUBLISHER: Springer-Verlag New York Inc., 175 Fifth Avenue, New York, NY, 10010, USA
Springer-Verlag GmbH & Co. KG, Heidelberger Platz 3, D-14197, Berlin, Germany
ISSN: 0079-6484 ISBN: 3-540-67220-6 (cloth)
DOCUMENT TYPE: Book
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology
BIOSYSTEMATIC NAMES: Organisms
ORGANISMS: organism (Organisms)
CHEMICALS & BIOCHEMICALS: *collagen type I*--conformation, structure
METHODS & EQUIPMENT: collagen type 1 invasion assay--analytical method
MISCELLANEOUS TERMS: *angiogenesis*; cell invasion; morphogenesis; Book Chapter
CONCEPT CODES:
02502 Cytology and Cytochemistry-General
10060 Biochemical Studies-General
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
BIOSYSTEMATIC CODES:
00500 Organisms-Unspecified

24/5/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12731815 BIOSIS NO.: 200000485317
Halofuginone: From veterinary use to human therapy.
AUTHOR: Pines Mark(a); Vlodavsky Israel; Nagler Arnon
AUTHOR ADDRESS: (a)Volcani Center, Institute of Animal Science, ARO, Bet Dagan, 50250**Israel
JOURNAL: Drug Development Research 50 (3-4):p371-378 Jul-Aug, 2000
MEDIUM: print
ISSN: 0272-4391
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: At present, halofuginone is the only known inhibitor of collagen synthesis that is type specific. Halofuginone was found to inhibit collagen alpha1 (I) gene expression and collagen synthesis in vitro in cell cultures and in various animal models in vivo characterized by excessive deposition of collagen, which results in fibrosis. Toxicity studies both in animals and in normal volunteers revealed no major side effects. Halofuginone was successfully used topically in a patient with chronic graft-versus-host disease and at present is being tested in a clinical trial of patients with scleroderma. Collagen is an important component of the stroma and is involved in endothelial cell migration and assembly to form and recruit new blood vessels-*angiogenesis*. Both stromal support and *angiogenesis* are critical for tumor growth. Based on this rationale, using various tumor models such as bladder carcinoma, prostate cancer, and glioma, we demonstrated that inhibition of collagen alpha1(I) gene expression by halofuginone caused inhibition of *angiogenesis*, which resulted in arrest of tumor growth. Thus, inhibition of collagen type I synthesis provides an attractive new target for cancer therapy. Many of the possible targets for halofuginone therapy pose enormous clinical problems, most of them without solutions. The

ability of extremely low concentrations of halofuginone, given orally, locally or injected intraperitoneally, to inhibit collagen alpha1(I) synthesis specifically and transiently at the transcriptional level suggests that this compound fulfills the criteria for a successful and effective antifibrotic and anticancer therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS ETC: endothelial cell--migration; tumor--growth
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: bladder carcinoma--neoplastic disease, urologic disease; chronic graft-vs-host disease--immune system disease; fibrosis--connective tissue disease; glioma--neoplastic disease, nervous system disease; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease; scleroderma--connective tissue disease, integumentary system disease
CHEMICALS & BIOCHEMICALS: collagen--synthesis; *collagen type I*--synthesis; halofuginone--antineoplastic-drug, collagen synthesis inhibitor, intraperitoneal, oral; animal collagen-alpha-1(I) gene (Animalia)--gene expression
METHODS & EQUIPMENT: cancer therapy--therapeutic method
MISCELLANEOUS TERMS: *angiogenesis*--inhibition
ALTERNATE INDEXING: Bladder Neoplasms (MeSH); Carcinoma (MeSH); Graft vs Host Disease (MeSH); Fibrosis (MeSH); Glioma (MeSH); Prostatic Neoplasms (MeSH)
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
03506 Genetics and Cytogenetics-Animal
03508 Genetics and Cytogenetics-Human
12512 Pathology, General and Miscellaneous-Therapy (1971-)
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
18006 Bones, Joints, Fasciae, Connective and Adipose Tissue-Pathology
18506 Integumentary System-Pathology
20506 Nervous System-Pathology
22002 Pharmacology-General
22005 Pharmacology-Clinical Pharmacology (1972-)
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
33000 Animalia-Unspecified
86215 Hominidae

24/5/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12498350 BIOSIS NO.: 200000251852
A novel effect of polymorphonuclear leukocytes in the facilitation of *angiogenesis*.
AUTHOR: Yasuda Masako; Shimizu Shunichi; Tokuyama Shogo; Watanabe Tohru; Kiuchi Yuji; Yamamoto Toshinori(a)
AUTHOR ADDRESS: (a)Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Showa University, 1-5-8 Haranodai, Shinagawa-ku, Tokyo, 142-8555**Japan
JOURNAL: Life Sciences 66 (21):p2113-2121 April 14, 2000
ISSN: 0024-3205

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The purpose of this study was to examine whether the adhesion of polymorphonuclear leukocytes (PMNs) to endothelial cells and/or reactive oxygen species (ROS) released from PMNs are responsible for inducing *angiogenesis*. *Angiogenesis* was assessed by the tube formation using endothelial cells obtained from bovine thoracic aorta (BAECs) grown on a layer of collagen type I. Addition of PMNs to BAECs weakly induced *angiogenesis*. The *angiogenesis* induced by PMNs alone was further enhanced by treatment of the PMNs with N-formyl-methionyl-leucyl-phenylalanine (FMLP), a selective activator of PMN. The involvement of PMN adhesion to BAECs via adhesion molecules in *angiogenesis* was investigated by using monoclonal antibodies against E-selectin and intercellular adhesion molecule-1 (ICAM-1). These antibodies blocked both the PMN adhesion to BAECs and the enhancement of *angiogenesis* induced by FMLP-treated PMNs. Furthermore, the enhancement of *angiogenesis* by FMLP-treated PMNs was blocked by catalase, a scavenging enzyme of H2O2, but not by superoxide dismutase (SOD). These results suggest that PMNs induce *angiogenesis* in vitro, and that the mechanism of stimulation of *angiogenesis* by PMNs may involve the adherence of PMNs to endothelial cells via E-selectin and ICAM-1, and H2O2, but not superoxide. Thus, activated PMNs in pathological states may only induce tissue injury, but may also function as regulators of *angiogenesis*.

REGISTRY NUMBERS: 59880-97-6: N-FORMYL-METHIONYL-LEUCYL-PHENYLALANINE; 9001-05-2: CATALASE; 7722-84-1: HYDROGEN PEROXIDE; 9054-89-1: SUPEROXIDE DISMUTASE
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation)
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Wistar rat (Muridae)--male
ORGANISMS: PARTS ETC: endothelial cells; polymorphonuclear leukocytes--adhesion, blood and lymphatics, immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: E-selectin; N-formyl-methionyl-leucyl-phenylalanine {FMLP}--polymorphonuclear leukocyte activator; catalase; *collagen type I*; hydrogen peroxide --scavenging enzyme; intercellular adhesion molecule-1 {ICAM-1}; reactive oxygen species {ROS}; superoxide dismutase {SOD
MISCELLANEOUS TERMS: *angiogenesis*
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
10802 Enzymes-General and Comparative Studies; Coenzymes
15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
86375 Muridae

24/5/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12058789 BIOSIS NO.: 199900339308
***Angiogenesis* during liver carcinogenesis: An in vivo and in vitro experimental study.**
AUTHOR: Nejjari Mimoun(a); Gouysse Geraldine(a); Dumortier Jerome(a); Pereira Adelino(a); Anderson Wena(a); Jacquier Marie-France(a);

Chayvialle Jean-Alain(a) [redacted]coazec Jean-Yves(a)
AUTHOR ADDRESS: (a)INSERM [redacted], Hosp E Herriot, Lyon**France
JOURNAL: Gastroenterology 116 (4 PART 2):pA1254 April, 1999
CONFERENCE/MEETING: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999
SPONSOR: American Gastroenterological Association
ISSN: 0016-5085
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 9041-92-3: ALPHA-1-ANTITRYPSIN
DESCRIPTORS:
MAJOR CONCEPTS: Digestive System (Ingestion and Assimilation); Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: rat (Muridae)--newborn; HepG2 cell line (Hominidae)--human hepatocarcinoma cells; HUVEC cell line (Hominidae)--human umbilical vein endothelial cells
ORGANISMS: PARTS ETC: myofibroblasts--muscular system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: albumin; alpha-fetoprotein; alpha-1-antitrypsin; *collagen type I*; collagen type IV; fibronectin; laminin-1; tenascin; type 19 cytokeratin; type 7 cytokeratin; type 8 cytokeratin
MISCELLANEOUS TERMS: *angiogenesis*; cell-cell interactions; liver carcinogenesis; Meeting Abstract
CONCEPT CODES:
24002 Neoplasms and Neoplastic Agents-General
02508 Cytology and Cytochemistry-Human
10060 Biochemical Studies-General
14001 Digestive System-General; Methods
14501 Cardiovascular System-General; Methods
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
86215 Hominidae
86375 Muridae

24/5/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11989869 BIOSIS NO.: 199900270388
Halofuginone: An inhibitor of collagen type I synthesis and of *angiogenesis* inhibits brain tumor growth in vivo.
AUTHOR: Siegal Tali(a); Nagler Arnon(a); Pines Mark; Vlodavsky Israel
AUTHOR ADDRESS: (a)Jerusalem**Israel
JOURNAL: Neurology 52 (6 SUPPL. 2):pA424 April 12, 1999
CONFERENCE/MEETING: 51st Annual Meeting of the American Academy of Neurology Toronto, Ontario, Canada April 17-24, 1999
SPONSOR: American Academy of Neurology
ISSN: 0028-3878
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System (Neural Coordination); Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Fischer rat (Muridae)--animal model
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

DISEASES: brain tumor--[redacted]plastic disease, treatment, ne[redacted]us system disease
CHEMICALS & BIOCHEMICALS: *collagen type I*--synthesis inhibition; halofuginone--antineoplastic-drug
MISCELLANEOUS TERMS: *angiogenesis*--inhibition; tumor growth--inhibition; Meeting Abstract; Meeting Poster
ALTERNATE INDEXING: Brain Neoplasms (MeSH)
CONCEPT CODES:
22002 Pharmacology-General
12512 Pathology, General and Miscellaneous-Therapy (1971-)
20501 Nervous System-General; Methods
24002 Neoplasms and Neoplastic Agents-General
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10060 Biochemical Studies-General
BIOSYSTEMATIC CODES:
86375 Muridae

24/5/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11878870 BIOSIS NO.: 199900124979
Cellular and molecular mechanisms of tissue repair.
AUTHOR: Scharffetter-Kochanek K(a); Klein P; Krieg T
AUTHOR ADDRESS: (a)Dep. Dermatol., Univ. Cologne, Joseph-Stelzmann-Str. 9, D-50924 Cologne**Germany
JOURNAL: Basic Research in Cardiology 93 (SUPPL. 3):p1-3 1998
ISSN: 0300-8428
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 153-87-7Q: INTEGRIN; 60791-49-3Q: INTEGRIN
DESCRIPTORS:
MAJOR CONCEPTS: Cell Biology
BIOSYSTEMATIC NAMES: Animalia
ORGANISMS: animal (Animalia)--animal model
ORGANISMS: PARTS ETC: *collagen type I*; extracellular matrix; human dermal fibroblasts--migratory response; keratinocytes--integumentary system, migratory response; lymphocytes--blood and lymphatics, immune system; monocytes--blood and lymphatics, immune system; neutrophils--blood and lymphatics, immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals
CHEMICALS & BIOCHEMICALS: beta-1 integrin--expression, induction; beta-2 integrin--expression, induction; divalent cations; fibronectin ; intercellular adhesion molecule-1; recombinant platelet-derived growth factor; selectin; selectin ligands; transforming growth factor-beta 1--regulation; vitronectin
MISCELLANEOUS TERMS: *angiogenesis*; cell migration; cell-cell interactions; cell-matrix interactions; tissue repair--cellular mechanisms, molecular mechanisms; wound healing
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
10060 Biochemical Studies-General
11107 Anatomy and Histology, General and Comparative-Regeneration and Transplantation (1971-)
15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods
17002 Endocrine System-General
18001 Bones, Joints, Fasciae, Connective and Adipose Tissue-General; Methods
BIOSYSTEMATIC CODES:
33000 Animalia-Unspecified

24/5/9 (Item 9 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

11772455 BIOSIS NO.: 199900018564
Template for *angiogenesis*: VEGF-induced reorganization of the endothelial cell monolayer on collagen type I.
AUTHOR: Dawson N S; Granger H J
AUTHOR ADDRESS: Microcirculation Res. Inst., Tex. A and M Univ. Syst. Health Sci. Cent., College Station, TX 77843**USA
JOURNAL: Molecular Biology of the Cell 9 (SUPPL.):p314A Nov., 1998
CONFERENCE/MEETING: 38th Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 12-16, 1998
SPONSOR: American Society for Cell Biology
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Cardiovascular System (Transport and Circulation); Cell Biology; Development; Endocrine System (Chemical Coordination and Homeostasis)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: endothelial cell--circulatory system, differentiation, reorganization, monolayer
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: *collagen type I*; vascular endothelial growth factor
MISCELLANEOUS TERMS: *angiogenesis*; Meeting Abstract
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10060 Biochemical Studies-General
14501 Cardiovascular System-General; Methods
17002 Endocrine System-General
25502 Developmental Biology-Embryology-General and Descriptive
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
86215 Hominidae

24/5/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11517757 BIOSIS NO.: 199800299089
NF-kappaB mediates alphavbeta3 integrin-induced endothelial cell survival.
AUTHOR: Scatena Marta(a); Almeida Manuela; Chaisson Michelle L; Fausto Nelson; Nicosia Roberto F; Giachelli Cecilia M
AUTHOR ADDRESS: (a)Dep. Pathol., Univ. Washington, Box 357335, Seattle, WA **USA
JOURNAL: Journal of Cell Biology 141 (4):p1083-1093 May 18, 1998
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The alphavbeta3 integrin plays a fundamental role during the *angiogenesis* process by inhibiting endothelial cell apoptosis. However, the mechanism of inhibition is unknown. In this report, we show that integrin-mediated cell survival involves regulation of nuclear factor-kappa B (NF-kappaB) activity. Different extracellular matrix molecules were able to protect rat aorta-derived endothelial cells from apoptosis induced by serum withdrawal. Osteopontin and beta3 integrin ligation rapidly increased NF-kappaB activity as measured by gel shift and reporter activity. The p65 and p50 subunits were present in the

shifted complex. In contrast, collagen type I (a beta1-integrin ligand) did not induce NF-kappaB activity. The alphavbeta3 integrin was most important for osteopontin-mediated NF-kappaB induction and survival, since adding a neutralizing anti-beta3 integrin antibody blocked NF-kappaB activity and induced endothelial cell death when cells were plated on osteopontin. NF-kappaB was required for osteopontin- and vitronectin-induced survival since inhibition of NF-kappaB activity with nonphosphorylatable IkappaB completely blocked the protective effect of osteopontin and vitronectin. In contrast, NF-kappaB was not required for fibronectin, laminin, and collagen type I-induced survival. Activation of NF-kappaB by osteopontin depended on the small GTP-binding protein Ras and the tyrosine kinase Src, since NF-kappaB reporter activity was inhibited by Ras and Src dominant-negative mutants. In contrast, inhibition of MEK and P13-kinase did not affect osteopontin-induced NF-kappaB activation. These studies identify NF-kappaB as an important signaling molecule in alphavbeta3 integrin-mediated endothelial cell survival.

REGISTRY NUMBERS: 153-87-7Q: INTEGRIN; 60791-49-3Q: INTEGRIN
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: RAEC (Muridae)--rat aortic endothelial cells
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: alpha-v-beta-3 integrin; beta-3 integrin; *collagen type I*; fibronectin; laminin; mitogen activated protein kinase kinase--inhibition; osteopontin; phosphotidylinositol 3 kinase ; vitronectin; NF-kappa-B (nuclear factor-kappa-B); Ras protein; Src protein
MISCELLANEOUS TERMS: *angiogenesis*; apoptosis--inhibition; cell survival
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10060 Biochemical Studies-General
10802 Enzymes-General and Comparative Studies; Coenzymes
15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods
BIOSYSTEMATIC CODES:
86375 Muridae

24/5/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10899386 BIOSIS NO.: 199799520531
Immunomorphological characteristics of certain parameters of the stomach carcinoma invasion.
AUTHOR: Frank G A; Litvinova L V; Belous T A; Pugachev K K
AUTHOR ADDRESS: P.A. Herzen Mosc. Oncol. Res. Inst., Moscow**Russia
JOURNAL: Arkhiv Patologii 59 (2):p22-27 1997
ISSN: 0004-1955
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English
SUMMARY LANGUAGE: English

ABSTRACT: 25 cases of advanced stomach carcinoma were studied immunomorphologically with the use of the antibodies panel to the carcinoembryonic antigen and meconian antigen B-1, collagen types IV, I and III, laminin, Ki-67, P-105, factor VIII. Secretory and proliferative activity of tumor cells was shown unrelated to histological structure and degree of tumor differentiation. The more was proliferative activity the weaker was the secretory function. Formation of the basal membrane (BM), the degree of collagen formation and *angiogenesis* in the tubular adenocarcinoma did not depend on the differentiation level and the degree of tumor cells secretory activity. On the contrary, carcinoid component

was characterized by pr[redacted]nced *angiogenesis* and tender[redacted] to correlation between the degree of differentiation and the degree of BM formation. Stomach carcinoma is a heterogenous group of tumors whose various morphological features may have an independent prognostic value.

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Immune System (Chemical Coordination and Homeostasis); Oncology (Human Medicine, Medical Sciences)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
MISCELLANEOUS TERMS: Research Article; *ANGIOGENESIS*; BASAL MEMBRANE FORMATION; CARCINOEMBRYONIC ANTIGEN; COLLAGEN FORMATION; *COLLAGEN TYPE I*; COLLAGEN TYPE III; COLLAGEN TYPE IV; DIGESTIVE SYSTEM DISEASE; FACTOR VIII; IMMUNOMORPHOLOGICAL FEATURES; INVASIVE; KI-67; MECONIAN ANTIGEN B1; NEOPLASTIC DISEASE; P-105; STOMACH CARCINOMA; TUMOR BIOLOGY ; TUMOR CELL PROLIFERATION; TUMOR CELL SECRETORY ACTIVITY; TUMOR DIFFERENTIATION
CONCEPT CODES:
10060 Biochemical Studies-General
14001 Digestive System-General; Methods
24002 Neoplasms and Neoplastic Agents-General
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
86215 Hominidae
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Set	Items	Description
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S2	7	RD (unique items)
S3	0	S2 AND ANTAGONIST?
S4	1	S2 AND ANTIBOD?
S5	0	S7 AND TYPE I
S6	0	S2 AND TYPE I
S7	1088	COLLAGEN TYPE I
S8	20	S7 AND ANTAGONIST?
S9	10	RD (unique items)
S10	0	S8 AND DENATUR?
S11	2	S8 AND ANTIBOD?
S12	1	RD (unique items)
S13	0	S7 AND NON-PEPTIDIC COMPOUND
S14	6	S7 AND OLIGONUCLEOTIDE?
S15	3	RD (unique items)
S16	0	DENATURED COLLAGEN TYPE I
S17	0	DENATUR? COLLAGEN TYPE I
S18	2	REDUCED AFFINITY
S19	0	S18 AND S1
S20	2	S7 AND MONOCLONAL ANTIBOD?
S21	1	RD (unique items)
S22	86193	ANGIOGENESIS
S23	22	S22 AND S7
S24	11	RD (unique items)
S25	0	S24 AND ANTAGONIST?

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Completed processing all files
22 S23
4650062 INHIBIT?
S26 8 S23 AND INHIBIT?
?s s23 and inhibit?
22 S23
4650062 INHIBIT?
S27 8 S23 AND INHIBIT?

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>>>Duplicate detection is not supported for File 340.
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>>>Duplicate detection is not supported for File 349.

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28/5/1   (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)

13090401   BIOSIS NO.: 200100297550
The anti-angiogenic effect of halofuginone (Halo): *Inhibition* of collagen type I tube formation, matrix metalloproteinase-2 (MMP-2) activities and extracellular matrix (ECM) deposition.
AUTHOR: Nagler A(a); Elkin E; Miao H-Q; Reich R; Pines M; Vlodavsky I
AUTHOR ADDRESS: (a)BMT, Hadassah**Israel
JOURNAL: Blood 96 (11 Part 1):p34a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: *Angiogenesis* is essential for the growth and spread of hematooncological tumors. It is a multifactorial process involving type I collagen tube formation which directs the migration and assembly of endothelial cells, MMP-2 degradation of ECM proteins including collagen and new capillary basement membrane (BM)-like ECM deposition. Halo, a low molecular weight (495Da) quinazolinone alkaloid was previously shown by us to *inhibit* collagen alpha1 (I) gene expression and synthesis. We therefore hypothesized that Halo may *inhibit* *angiogenesis*. We evaluated the potential antiangiogenic effect of Halo both in vitro and in vivo using several assays: 1) Capillary-like tube formation with Bovine aortic and human umbilical endothelial cells. 2) Rat aortic ring microvessel formation and 3) Murine micropocket bFGF induced corneal *angiogenesis*. In vitro in the presence of Halo (50 ng/ml) both bovine and human endothelial cells lost their ability to form new capillary vessels and appeared as unorganized cell aggregates. Similarly Halo (100ng/ml) completely *inhibited* microvessel formation from rat aortic rings embedded in collagen type I gel. As collagen type I is one of the major constituents of the stroma we evaluated the effect of Halo on ECM deposition by cultured vascular endothelial cells assessed by incorporation of radiolabeled sulfate. Eighty five percent *inhibition* of ECM deposition was observed in cultures incubated with 50ng/ml Halo. In addition microscopic examinations of the denuded culture dishes revealed a very thin or no ECM. We next evaluated the effect of Halo on MMP-2 enzymatic activity by vascular endothelial cells and demonstrated an almost complete *inhibition* of MMP-2 expression and enzymatic activity as well as BM invasion by 100ng/ml Halo. Finally, in vivo Halo administered either P.O (5mg/kg) or I.P. (2mg/mouse/day) for 7 days caused profound *inhibition* of bFGF induced corneal neovascularization in the murine micropocket corneal *angiogenesis* model (the area of neovascularization was reduced from 1.7+0.3 mm2 to 0.6+0.2 mm2 in the control and Halo (either P.O or I.P) treated mice, respectively. In

summary, Halo *inhibits* several steps in the angiogenetic process: MMP-2 expression and BM invasion, capillary-like tube formation and vascular sprouting as well as deposition of subendothelial ECM and finally bFGF induced neovascularization in vivo. This makes Halo a promising candidate for further evaluation in anti-angiogenic therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE; 146480-35-5: MATRIX METALLOPROTEINASE-2
DESCRIPTORS:
MAJOR CONCEPTS: Immune System (Chemical Coordination and Homeostasis); Pharmacology
BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: bovine (Bovidae); human (Hominidae); mouse (Muridae); rat (Muridae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Artiodactyls; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: *collagen type I*; halofuginone--anti-angiogenic effect, antineoplastic-drug; matrix metalloproteinase-2
MISCELLANEOUS TERMS: *angiogenesis*; collagen type I tube formation--*inhibition*; extracellular matrix deposition; Meeting Abstract
CONCEPT CODES:
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10802 Enzymes-General and Comparative Studies; Coenzymes
12512 Pathology, General and Miscellaneous-Therapy (1971-)
22002 Pharmacology-General
22005 Pharmacology-Clinical Pharmacology (1972-)
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
85715 Bovidae
86215 Hominidae
86375 Muridae

28/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12731815 BIOSIS NO.: 200000485317
Halofuginone: From veterinary use to human therapy.
AUTHOR: Pines Mark(a); Vlodavsky Israel; Nagler Arnon
AUTHOR ADDRESS: (a)Volcani Center, Institute of Animal Science, ARO, Bet Dagan, 50250**Israel
JOURNAL: Drug Development Research 50 (3-4):p371-378 Jul-Aug, 2000
MEDIUM: print
ISSN: 0272-4391
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: At present, halofuginone is the only known *inhibitor* of collagen synthesis that is type specific. Halofuginone was found to *inhibit* collagen alpha1 (I) gene expression and collagen synthesis in vitro in cell cultures and in various animal models in vivo characterized by excessive deposition of collagen, which results in fibrosis. Toxicity studies both in animals and in normal volunteers revealed no major side effects. Halofuginone was successfully used topically in a patient with chronic graft-versus-host disease and at present is being tested in a clinical trial of patients with scleroderma. Collagen is an important component of the stroma and is involved in endothelial cell migration and

assembly to form and recruit new blood vessels-*angiogenesis*. Both stromal support and *angiogenesis* are critical for tumor growth. Based on this rationale, using various tumor models such as bladder carcinoma, prostate cancer, and glioma, we demonstrated that *inhibition* of collagen alpha1(I) gene expression by halofuginone caused *inhibition* of *angiogenesis*, which resulted in arrest of tumor growth. Thus, *inhibition* of collagen type I synthesis provides an attractive new target for cancer therapy. Many of the possible targets for halofuginone therapy pose enormous clinical problems, most of them without solutions. The ability of extremely low concentrations of halofuginone, given orally, locally or injected intraperitoneally, to *inhibit* collagen alpha1(I) synthesis specifically and transiently at the transcriptional level suggests that this compound fulfills the criteria for a successful and effective antifibrotic and anticancer therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS ETC: endothelial cell--migration; tumor--growth
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: bladder carcinoma--neoplastic disease, urologic disease; chronic graft-vs-host disease--immune system disease; fibrosis--connective tissue disease; glioma--neoplastic disease, nervous system disease; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease; scleroderma--connective tissue disease, integumentary system disease
CHEMICALS & BIOCHEMICALS: collagen--synthesis; *collagen type I*--synthesis; halofuginone--antineoplastic-drug, collagen synthesis *inhibitor*, intraperitoneal, oral; animal collagen-alpha-1(I) gene (Animalia)--gene expression
METHODS & EQUIPMENT: cancer therapy--therapeutic method
MISCELLANEOUS TERMS: *angiogenesis*--*inhibition*
ALTERNATE INDEXING: Bladder Neoplasms (MeSH); Carcinoma (MeSH); Graft vs Host Disease (MeSH); Fibrosis (MeSH); Glioma (MeSH); Prostatic Neoplasms (MeSH)
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
03506 Genetics and Cytogenetics-Animal
03508 Genetics and Cytogenetics-Human
12512 Pathology, General and Miscellaneous-Therapy (1971-)
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
18006 Bones, Joints, Fasciae, Connective and Adipose Tissue-Pathology
18506 Integumentary System-Pathology
20506 Nervous System-Pathology
22002 Pharmacology-General
22005 Pharmacology-Clinical Pharmacology (1972-)
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
33000 Animalia-Unspecified
86215 Hominidae

28/5/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11989869 BIOSIS NO.: 199900270388

Halofuginone: An *inhibito[redacted] of collagen type I synthesis a[redacted] of *angiogenesis* *inhibits* brain tumor growth in vivo.
AUTHOR: Siegal Tali(a); Nagler Arnon(a); Pines Mark; Vlodavsky Israel
AUTHOR ADDRESS: (a)Jerusalem**Israel
JOURNAL: Neurology 52 (6 SUPPL. 2):pA424 April 12, 1999
CONFERENCE/MEETING: 51st Annual Meeting of the American Academy of Neurology Toronto, Ontario, Canada April 17-24, 1999
SPONSOR: American Academy of Neurology
ISSN: 0028-3878
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System (Neural Coordination); Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Fischer rat (Muridae)--animal model
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
DISEASES: brain tumor--neoplastic disease, treatment, nervous system disease
CHEMICALS & BIOCHEMICALS: *collagen type I*--synthesis *inhibition*; halofuginone--antineoplastic-drug
MISCELLANEOUS TERMS: *angiogenesis*--*inhibition*; tumor growth--*inhibition*; Meeting Abstract; Meeting Poster
ALTERNATE INDEXING: Brain Neoplasms (MeSH)
CONCEPT CODES:
22002 Pharmacology-General
12512 Pathology, General and Miscellaneous-Therapy (1971-)
20501 Nervous System-General; Methods
24002 Neoplasms and Neoplastic Agents-General
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10060 Biochemical Studies-General
BIOSYSTEMATIC CODES:
86375 Muridae

28/5/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11517757 BIOSIS NO.: 199800299089
NF-kappaB mediates alphavbeta3 integrin-induced endothelial cell survival.
AUTHOR: Scatena Marta(a); Almeida Manuela; Chaisson Michelle L; Fausto Nelson; Nicosia Roberto F; Giachelli Cecilia M
AUTHOR ADDRESS: (a)Dep. Pathol., Univ. Washington, Box 357335, Seattle, WA **USA
JOURNAL: Journal of Cell Biology 141 (4):p1083-1093 May 18, 1998
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The alphavbeta3 integrin plays a fundamental role during the *angiogenesis* process by *inhibiting* endothelial cell apoptosis. However, the mechanism of *inhibition* is unknown. In this report, we show that integrin-mediated cell survival involves regulation of nuclear factor-kappa B (NF-kappaB) activity. Different extracellular matrix molecules were able to protect rat aorta-derived endothelial cells from apoptosis induced by serum withdrawal. Osteopontin and beta3 integrin ligation rapidly increased NF-kappaB activity as measured by gel shift and reporter activity. The p65 and p50 subunits were present in the shifted complex. In contrast, collagen type I (a beta1-integrin ligand) did not induce NF-kappaB activity. The alphavbeta3 integrin was most important for osteopontin-mediated NF-kappaB induction and survival,

since adding a neutraliz[redacted] anti-beta3 integrin antibody [redacted]cked NF-kappaB activity and induced endothelial cell death when cells were plated on osteopontin. NF-kappaB was required for osteopontin- and vitronectin-induced survival since *inhibition* of NF-kappaB activity with nonphosphorylatable IkappaB completely blocked the protective effect of osteopontin and vitronectin. In contrast, NF-kappaB was not required for fibronectin, laminin, and collagen type I-induced survival. Activation of NF-kappaB by osteopontin depended on the small GTP-binding protein Ras and the tyrosine kinase Src, since NF-kappaB reporter activity was *inhibited* by Ras and Src dominant-negative mutants. In contrast, *inhibition* of MEK and P13-kinase did not affect osteopontin-induced NF-kappaB activation. These studies identify NF-kappaB as an important signaling molecule in alphavbeta3 integrin-mediated endothelial cell survival.

REGISTRY NUMBERS: 153-87-7Q: INTEGRIN; 60791-49-3Q: INTEGRIN
DESCRIPTORS:
  MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology
  BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
  ORGANISMS: RAEC (Muridae)--rat aortic endothelial cells
  BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
  CHEMICALS & BIOCHEMICALS: alpha-v-beta-3 integrin; beta-3 integrin; *collagen type I*; fibronectin; laminin; mitogen activated protein kinase kinase--*inhibition*; osteopontin; phosphotidylinositol 3 kinase; vitronectin; NF-kappa-B {nuclear factor-kappa-B}; Ras protein; Src protein
  MISCELLANEOUS TERMS: *angiogenesis*; apoptosis--*inhibition*; cell survival
CONCEPT CODES:
  02506 Cytology and Cytochemistry-Animal
  10060 Biochemical Studies-General
  10802 Enzymes-General and Comparative Studies; Coenzymes
  15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods
BIOSYSTEMATIC CODES:
  86375 Muridae
?s inhibit? and collagen type I
  4650062 INHIBIT?
  1088 COLLAGEN TYPE I
S29 264 INHIBIT? AND COLLAGEN TYPE I
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S4	1	S2 AND ANTIBOD?
S5	0	S7 AND TYPE I
S6	0	S2 AND TYPE I
S7	1088	COLLAGEN TYPE I
S8	20	S7 AND ANTAGONIST?

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S11          2   S8 AND ANTIBOD?
S12          1   RD (unique items)
S13          0   S7 AND NON-PEPTIDIC COMPOUND
S14          6   S7 AND OLIGONUCLEOTIDE?
S15          3   RD (unique items)
S16          0   DENATURED COLLAGEN TYPE I
S17          0   DENATUR? COLLAGEN TYPE I
S18          2   REDUCED AFFINITY
S19          0   S18 AND S1
S20          2   S7 AND MONOCLONAL ANTIBOD?
S21          1   RD (unique items)
S22      86193   ANGIOGENESIS
S23         22   S22 AND S7
S24         11   RD (unique items)
S25          0   S24 AND ANTAGONIST?
S26          8   S23 AND INHIBIT?
S27          8   S23 AND INHIBIT?
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S29        264   INHIBIT? AND COLLAGEN TYPE I
S30        131   RD (unique items)
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             131  S30
           86193  ANGIOGENESIS
     S31       4  S30 AND ANGIOGENESIS
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>>>Duplicate detection is not supported for File 447.
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 32/5/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

13090401   BIOSIS NO.: 200100297550
```
The anti-angiogenic effect of halofuginone (Halo): *Inhibition* of collagen type I tube formation, matrix metalloproteinase-2 (MMP-2) activities and extracellular matrix (ECM) deposition.

AUTHOR: Nagler A(a); Elkin E; Miao H-Q; Reich R; Pines M; Vlodavsky I
AUTHOR ADDRESS: (a)BMT, Hadassah**Israel
JOURNAL: Blood 96 (11 Part 1):p34a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: *Angiogenesis* is essential for the growth and spread of hematooncological tumors. It is a multifactorial process involving type I collagen tube formation which directs the migration and assembly of endothelial cells, MMP-2 degradation of ECM proteins including collagen and new capillary basement membrane (BM)-like ECM deposition. Halo, a low molecular weight (495Da) quinazolinone alkaloid was previously shown by us to *inhibit* collagen alpha1 (I) gene expression and synthesis. We therefore hypothesized that Halo may *inhibit* *angiogenesis*. We evaluated the potential antiangiogenic effect of Halo both in vitro and

in vivo using several as[redacted]s: 1) Capillary-like tube form[redacted]on with Bovine aortic and human umbilical endothelial cells. 2) Ra[redacted] aortic ring microvessel formation and 3) Murine micropocket bFGF induced corneal *angiogenesis*. In vitro in the presence of Halo (50 ng/ml) both bovine and human endothelial cells lost their ability to form new capillary vessels and appeared as unorganized cell aggregates. Similarly Halo (100ng/ml) completely *inhibited* microvessel formation from rat aortic rings embedded in collagen type I gel. As collagen type I is one of the major constituents of the stroma we evaluated the effect of Halo on ECM deposition by cultured vascular endothelial cells assessed by incorporation of radiolabeled sulfate. Eighty five percent *inhibition* of ECM deposition was observed in cultures incubated with 50ng/ml Halo. In addition microscopic examinations of the denuded culture dishes revealed a very thin or no ECM. We next evaluated the effect of Halo on MMP-2 enzymatic activity by vascular endothelial cells and demonstrated an almost complete *inhibition* of MMP-2 expression and enzymatic activity as well as BM invasion by 100ng/ml Halo. Finally, in vivo Halo administered either P.O (5mg/kg) or I.P. (2mg/mouse/day) for 7 days caused profound *inhibition* of bFGF induced corneal neovascularization in the murine micropocket corneal *angiogenesis* model (the area of neovascularization was reduced from 1.7+0.3 mm2 to 0.6+0.2 mm2 in the control and Halo (either P.O or I.P) treated mice, respectively. In summary, Halo *inhibits* several steps in the angiogenetic process: MMP-2 expression and BM invasion, capillary-like tube formation and vascular sprouting as well as deposition of subendothelial ECM and finally bFGF induced neovascularization in vivo. This makes Halo a promising candidate for further evaluation in anti-angiogenic therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE; 146480-35-5: MATRIX METALLOPROTEINASE-2
DESCRIPTORS:
MAJOR CONCEPTS: Immune System (Chemical Coordination and Homeostasis); Pharmacology
BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: bovine (Bovidae); human (Hominidae); mouse (Muridae); rat (Muridae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Artiodactyls; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: *collagen type I*; halofuginone--anti-angiogenic effect, antineoplastic-drug; matrix metalloproteinase-2
MISCELLANEOUS TERMS: *angiogenesis*; collagen type I tube formation--*inhibition*; extracellular matrix deposition; Meeting Abstract
CONCEPT CODES:
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10802 Enzymes-General and Comparative Studies; Coenzymes
12512 Pathology, General and Miscellaneous-Therapy (1971-)
22002 Pharmacology-General
22005 Pharmacology-Clinical Pharmacology (1972-)
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
85715 Bovidae
86215 Hominidae
86375 Muridae

32/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12731815 BIOSIS NO.: 200000485317

Halofuginone: From veterin[redacted] use to human therapy.

AUTHOR: Pines Mark(a); Vlodavsky Israel; Nagler Arnon
AUTHOR ADDRESS: (a)Volcani Center, Institute of Animal Science, ARO, Bet Dagan, 50250**Israel

JOURNAL: Drug Development Research 50 (3-4):p371-378 Jul-Aug, 2000
MEDIUM: print
ISSN: 0272-4391
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: At present, halofuginone is the only known *inhibitor* of collagen synthesis that is type specific. Halofuginone was found to *inhibit* collagen alpha1 (I) gene expression and collagen synthesis in vitro in cell cultures and in various animal models in vivo characterized by excessive deposition of collagen, which results in fibrosis. Toxicity studies both in animals and in normal volunteers revealed no major side effects. Halofuginone was successfully used topically in a patient with chronic graft-versus-host disease and at present is being tested in a clinical trial of patients with scleroderma. Collagen is an important component of the stroma and is involved in endothelial cell migration and assembly to form and recruit new blood vessels-*angiogenesis*. Both stromal support and *angiogenesis* are critical for tumor growth. Based on this rationale, using various tumor models such as bladder carcinoma, prostate cancer, and glioma, we demonstrated that *inhibition* of collagen alpha1(I) gene expression by halofuginone caused *inhibition* of *angiogenesis*, which resulted in arrest of tumor growth. Thus, *inhibition* of collagen type I synthesis provides an attractive new target for cancer therapy. Many of the possible targets for halofuginone therapy pose enormous clinical problems, most of them without solutions. The ability of extremely low concentrations of halofuginone, given orally, locally or injected intraperitoneally, to *inhibit* collagen alpha1(I) synthesis specifically and transiently at the transcriptional level suggests that this compound fulfills the criteria for a successful and effective antifibrotic and anticancer therapy.

REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS ETC: endothelial cell--migration; tumor--growth
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: bladder carcinoma--neoplastic disease, urologic disease; chronic graft-vs-host disease--immune system disease; fibrosis--connective tissue disease; glioma--neoplastic disease, nervous system disease; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease; scleroderma--connective tissue disease, integumentary system disease
CHEMICALS & BIOCHEMICALS: collagen--synthesis; *collagen type I*--synthesis; halofuginone--antineoplastic-drug, collagen synthesis *inhibitor*, intraperitoneal, oral; animal collagen-alpha-1(I) gene (Animalia)--gene expression
METHODS & EQUIPMENT: cancer therapy--therapeutic method
MISCELLANEOUS TERMS: *angiogenesis*--*inhibition*
ALTERNATE INDEXING: Bladder Neoplasms (MeSH); Carcinoma (MeSH); Graft vs Host Disease (MeSH); Fibrosis (MeSH); Glioma (MeSH); Prostatic Neoplasms (MeSH)
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
03506 Genetics and Cytogenetics-Animal
03508 Genetics and Cytogenetics-Human

12512 Pathology, General and Miscellaneous-Therapy (1971-)
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
18006 Bones, Joints, Fasciae, Connective and Adipose Tissue-Pathology
18506 Integumentary System-Pathology
20506 Nervous System-Pathology
22002 Pharmacology-General
22005 Pharmacology-Clinical Pharmacology (1972-)
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
33000 Animalia-Unspecified
86215 Hominidae

32/5/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11989869 BIOSIS NO.: 199900270388
Halofuginone: An *inhibitor* of collagen type I synthesis and of *angiogenesis* *inhibits* brain tumor growth in vivo.
AUTHOR: Siegal Tali(a); Nagler Arnon(a); Pines Mark; Vlodavsky Israel
AUTHOR ADDRESS: (a)Jerusalem**Israel
JOURNAL: Neurology 52 (6 SUPPL. 2):pA424 April 12, 1999
CONFERENCE/MEETING: 51st Annual Meeting of the American Academy of Neurology Toronto, Ontario, Canada April 17-24, 1999
SPONSOR: American Academy of Neurology
ISSN: 0028-3878
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 55837-20-2: HALOFUGINONE
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System (Neural Coordination); Pharmacology; Tumor Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Fischer rat (Muridae)--animal model
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
DISEASES: brain tumor--neoplastic disease, treatment, nervous system disease
CHEMICALS & BIOCHEMICALS: *collagen type I*--synthesis *inhibition*; halofuginone--antineoplastic-drug
MISCELLANEOUS TERMS: *angiogenesis*--*inhibition*; tumor growth--*inhibition*; Meeting Abstract; Meeting Poster
ALTERNATE INDEXING: Brain Neoplasms (MeSH)
CONCEPT CODES:
22002 Pharmacology-General
12512 Pathology, General and Miscellaneous-Therapy (1971-)
20501 Nervous System-General; Methods
24002 Neoplasms and Neoplastic Agents-General
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10060 Biochemical Studies-General
BIOSYSTEMATIC CODES:
86375 Muridae

32/5/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11517757 BIOSIS NO.: 199800299089
NF-kappaB mediates alphavbeta3 integrin-induced endothelial cell survival.

AUTHOR: Scatena Marta(a); A[redacted]eida Manuela; Chaisson Michelle[redacted]; Fausto Nelson; Nicosia Roberto F; Giachelli Cecilia M
AUTHOR ADDRESS: (a)Dep. Pathol., Univ. Washington, Box 357335, Seattle, WA **USA
JOURNAL: Journal of Cell Biology 141 (4):p1083-1093 May 18, 1998
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The alphavbeta3 integrin plays a fundamental role during the *angiogenesis* process by *inhibiting* endothelial cell apoptosis. However, the mechanism of *inhibition* is unknown. In this report, we show that integrin-mediated cell survival involves regulation of nuclear factor-kappa B (NF-kappaB) activity. Different extracellular matrix molecules were able to protect rat aorta-derived endothelial cells from apoptosis induced by serum withdrawal. Osteopontin and beta3 integrin ligation rapidly increased NF-kappaB activity as measured by gel shift and reporter activity. The p65 and p50 subunits were present in the shifted complex. In contrast, collagen type I (a beta1-integrin ligand) did not induce NF-kappaB activity. The alphavbeta3 integrin was most important for osteopontin-mediated NF-kappaB induction and survival, since adding a neutralizing anti-beta3 integrin antibody blocked NF-kappaB activity and induced endothelial cell death when cells were plated on osteopontin. NF-kappaB was required for osteopontin- and vitronectin-induced survival since *inhibition* of NF-kappaB activity with nonphosphorylatable IkappaB completely blocked the protective effect of osteopontin and vitronectin. In contrast, NF-kappaB was not required for fibronectin, laminin, and collagen type I-induced survival. Activation of NF-kappaB by osteopontin depended on the small GTP-binding protein Ras and the tyrosine kinase Src, since NF-kappaB reporter activity was *inhibited* by Ras and Src dominant-negative mutants. In contrast, *inhibition* of MEK and P13-kinase did not affect osteopontin-induced NF-kappaB activation. These studies identify NF-kappaB as an important signaling molecule in alphavbeta3 integrin-mediated endothelial cell survival.

REGISTRY NUMBERS: 153-87-7Q: INTEGRIN; 60791-49-3Q: INTEGRIN
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: RAEC (Muridae)--rat aortic endothelial cells
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: alpha-v-beta-3 integrin; beta-3 integrin; *collagen type I*; fibronectin; laminin; mitogen activated protein kinase kinase--*inhibition*; osteopontin; phosphotidylinositol 3 kinase; vitronectin; NF-kappa-B (nuclear factor-kappa-B); Ras protein; Src protein
MISCELLANEOUS TERMS: *angiogenesis*; apoptosis--*inhibition*; cell survival
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10060 Biochemical Studies-General
10802 Enzymes-General and Comparative Studies; Coenzymes
15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods
BIOSYSTEMATIC CODES:
86375 Muridae
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